Report No. NADC-91053-60

PHYSIOLOGIC "TRANSECTION" OF THE BRAIN STEM IN HEALTHY HUMANS AND THE NEUROLOGIC BASIS OF UNCONSCIOUSNESS

James E. Whinnery, Ph.D., M.D.
Air Vehicle and Crew Systems Technology Department (Code 602C)
NAVAL AIR DEVELOPMENT CENTER
Warminster, PA 18974-5000

10 FEBRUARY 1990

FINAL REPORT
Period Covering January 1988 to February 1990

Approved for Public Release; Distribution is Unlimited

Prepared for
Air Vehicle and Crew Systems Technology Department (Code 602C)
NAVAL AIR DEVELOPMENT CENTER
Warminster, PA 18974-5000

NOTICES

REPORT NUMBERING SYSTEM — The numbering of technical project reports issued by the Naval Air Development Center is arranged for specific identification purposes. Each number consists of the Center acronym, the calendar year in which the number was assigned, the sequence number of the report within the specific calendar year, and the official 2-digit correspondence code of the Command Officer or the Functional Department responsible for the report. For example: Report No. NADC-88020-60 indicates the twentieth Center report for the year 1988 and prepared by the Air Vehicle and Crew Systems Technology Department. The numerical codes are as follows:

CODE	OFFICE OR DEPARTMENT
00	Commander, Naval Air Development Center
01	Technical Director, Naval Air Development Center
05	Computer Department
10	AntiSubmarine Warfare Systems Department
20	Tactical Air Systems Department
30	Warfare Systems Analysis Department
40	Communication Navigation Technology Department
50	Mission Avionics Technology Department
60	Air Vehicle & Crew Systems Technology Department
70	Systems & Software Technology Department
80	Engineering Support Group
90	Test & Evaluation Group

PRODUCT ENDORSEMENT — The discussion or instructions concerning commercial products herein do not constitute an endorsement by the Government nor do they convey or imply the license or right to use such products.

Reviewed By: James E. Whinnery Ph.D., M.D. Date: 4 July 1991
Branch Head

Reviewed By: L.H. Frank Ph.D. Date: 24 JUL 91
Division Head

Reviewed By: W.A. Smith Date: 25 July 91
Director/Deputy Director

UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

1a REPORT SECURITY CLASSIFICATION: Unclassified	1b RESTRICTIVE MARKINGS
2a SECURITY CLASSIFICATION AUTHORITY	3 DISTRIBUTION/AVAILABILITY OF REPORT: Approved for Public Release; Distribution is Unlimited
2b DECLASSIFICATION/DOWNGRADING SCHEDULE	
4 PERFORMING ORGANIZATION REPORT NUMBER(S): NADC-91053-60	5 MONITORING ORGANIZATION REPORT NUMBER(S)
6a NAME OF PERFORMING ORGANIZATION: Air Vehicle and Crew Systems Technology Department; 6b OFFICE SYMBOL (If applicable): 6020	7a NAME OF MONITORING ORGANIZATION
6c ADDRESS (City, State, and ZIP Code): NAVAL AIR DEVELOPMENT CENTER Warminster, PA 18974-5000	7b ADDRESS (City, State, and ZIP Code)
8a NAME OF FUNDING/SPONSORING ORGANIZATION: Air Vehicle and Crew Systems Technology Dept.; 8b OFFICE SYMBOL (If applicable): 6020	9 PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c ADDRESS (City, State, and ZIP Code): NAVAL AIR DEVELOPMENT CENTER Warminster, PA 1897--5000	10 SOURCE OF FUNDING NUMBERS: PROGRAM ELEMENT NO; PROJECT NO; TASK NO; WORK UNIT ACCESSION NO

11 TITLE (Include Security Classification)
Physiologic "Transection" Of The Brain Stem In Healthy Humans And The Neurologic Basis Of Unconsciousness

12 PERSONAL AUTHOR(S)

13a TYPE OF REPORT	13b TIME COVERED	14 DATE OF REPORT (Year, Month, Day)	15 PAGE COUNT
Final	FROM 1/88 TO 2/90	1990 February 10	

16 SUPPLEMENTARY NOTATION

17 COSATI CODES			18 SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	Unconsciousness, Acceleration, Fighter Aviation, Neurophysiology, Centrifuge
01	03	03	

19 ABSTRACT (Continue on reverse if necessary and identify by block number)

Investigation of the kinetic relationships of the symptom complex associated with abrupt onset ischemic insult of the central nervous system (CNS) in over 700 completely healthy humans has revealed considerable insight into the neurologic substrates underlying conscious function, its loss, and its recovery. Acceleration ($+G_z$)-induced CNS ischemia of a magnitude to alter conscious function (G-LOC) is associated with loss of

20 DISTRIBUTION/AVAILABILITY OF ABSTRACT	21 ABSTRACT SECURITY CLASSIFICATION	
☒ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT ☐ DTIC USERS	Unclassified	
22a NAME OF RESPONSIBLE INDIVIDUAL: James E. Whinnery Ph.D., M.D.	22b TELEPHONE (Include Area Code): 215-4.. -4023	22c OFFICE SYMBOL: 6020

DD Form 1473, JUN 86 — Previous editions are obsolete — SECURITY CLASSIFICATION OF THIS PAGE

S/N 0102-LF-014-6603 — UNCLASSIFIED

Block 19 (Contd)

vision, postural motor control, and memory along with induction of myoclonic convulsions, dreaming, and transient confusion/ disorientation. It is evident that regional ischemic differences are established within the CNS and these neurologic alterations suggest that a reversible physiologic "transection" of the brain stem results from $+G_z$-induced ischemia. Understanding this $+G_z$-induced ischemic phenomenon provides a unique opportunity to investigate normal human neurologic function. Such an understanding holds the promise to reduce or prevent the many losses of multi-million dollar fighter aircraft and numerous aircrew lives that continues to plague tactical aviation.

FIGURES

Considerable understanding of central nervous system (CNS) neurophysiology has resulted from surgical transection of the neuraxis in experimental animals at various levels within the brain stem. This understanding has been augmented by neurosurgical and neuropathologic clinical investigations in patient populations. Based on detailed observation of the effects of high sustained $+G_z$, it appears that reversible "transection" of the neuraxis can be accomplished in normal humans with the resulting characteristics revealing the nature and extent of the CNS ischemia/hypoxia insult. Such investigations have valuable potential for further enhancing our understanding of the complex neurophysiological function of the CNS.

I wish to suggest a mechanism for the loss of consciousness resulting from acute reduction of blood flow to the central nervous system (CNS) and recovery following the subsequent return of CNS blood flow. This mechanism is basic to our being and of considerable physiological interest. Indeed, you cannot die unless you lose consciousness which thereby makes understanding the mechanism involved of importance to all human beings since they will ultimately experience the phenomenon personally sooner or later.

It has been my privilege to have observed, videotape recorded, and carefully analyzed nearly 700 acceleration ($+G_z$) induced loss of consciousness (G-LOC) episodes in completely healthy humans over the past 13 years, having also personally experienced approximately 30 G-LOC episodes myself. Acceleration stress applied in the head-to-foot ($+G_z$) direction results in abrupt reduction in blood flow to the areas above the heart with pooling of blood below the heart. When the CNS is deprived of adequate perfusion, a series of events (the G-LOC syndrome) is observed that can be kinetically related based on the rate of onset of the ischemic insult and the rate of return of blood flow. [1] Just as chemical kinetics provides insight into the mechanism of a chemical reaction, so G-LOC kinetics can provide valuable information on the CNS mechanism of loss of consciousness.

Figure 1 illustrates the kinetically related characteristics resulting from rapid onset $+G_z$-stress producing G-LOC with complete loss of muscle tone. In healthy humans, safety mandates that the $+G_z$-stress be terminated immediately upon onset of G-LOC with return to a normal earth's $+1G_z$ gravitational field. A period of unconsciousness (absolute incapacitation) followed by a period of confusion and disorientation (relative incapacitation) ensues, the sum of the two (total incapacitation) ending with the return of responsiveness and purposeful movement. The absolute incapacitation period (on the average 12 seconds) can be further separated into a myoclonic convulsion free period and a myoclonic convulsion prone period. The myoclonic convulsions last approximately 4 seconds ending essentially coincident with the return of consciousness. Short dreams, which may frequently incorporate myoclonic movements into them, suggest a dream period is near the end of the absolute incapacitation period. The fact that the dream is memorable implies memory circuitry is revitalized prior to the return of consciousness. The induction of G-LOC is dependent on the $+G_z$-onset rate. The minimum time for G-LOC induction has been found to be 5.6 seconds. The resulting incapacitation and recovery characteristics are dependent on the onset rate (slower onset rate, longer incapacitation) and the offset rate (faster offset rate, shorter incapacitation). Careful modulation of the CNS ischemia can produce any or all of the symptoms.

Based on these kinetically related events, it is possible to construct a mechanism consistent with currently understood neurophysiological principles which underlie consciousness, its loss, and its recovery. It became evident from G-LOC analysis that in the post G-LOC period there was a frequent sense of just having awaken from a daydream. This close analogy with sleep, reinforced by the occurrence of memorable dreams, suggests that similar mechanisms and neurologic substrates exists for sleep and G-LOC. The suggested mechanism for the loss of consciousness and recovery is therefore central to linking research involving sleep, the clinically related neurologic consequences of altered CNS anatomy and physiology, and the permanent cessation of such human function. Although the neurophysiological changes associated with $+G_z$-induced loss of consciousness are triggered by

ischemia, it is possible that a variety of stimuli (neuroendocrine, hypoxia, trauma, disease) trigger loss or altered consciousness by the same fundamental inhibition-activation mechanism.

I would suggest that it is valuable to approach G-LOC considering it to be the core of physiological protection for the CNS, equivalent to the extent of the protection anatomically provided by encasement within the skull and vertebral column. The characteristics of $+G_z$ -stress are such that CNS blood flow is sequentially compromised from the top down and in a watershed pattern. This results in compromised perfusion beginning in the highest cortical centers sequentially isolating a more primitive CNS. The relationship of the anatomic structures key to consciousness are schematically depicted in Figure 2 relative to the $+G_z$-stress being applied as shown. The location of the physiologic "transection" can be controlled by the magnitude and characteristics of the $+G_z$-stress. Based on the currently investigated $+G_z$-profiles, the insult within the CNS must extend to at least the intrapontine level of the brain stem. This being a level which initially isolates the physiologic effects of the facilitory and inhibitory centers of the reticular formation.

The step-by-step G-LOC and recovery mechanism follows:

A. INDUCTION (Rapid onset to sustained high level of $+G_z$)

1. $+G_z$-REDUCED BLOOD FLOW TO THE CNS:
   - HIGHER CENTERS (CORTEX) FIRST AFFECTED.
   - LOWER CENTERS (BRAIN STEM) LAST AFFECTED.

2. ALTERED PERFUSION OF NEURONS RESULTS IN REDUCED FLOW, PERFUSION PRESSURE, OXYGEN, AND GLUCOSE TO NEURONS.

3. ISCHEMIC INDUCED LOCAL NEURONAL METABOLIC INHIBITION TRIGGERED BY IMPAIRED

PERFUSION EITHER:

- INDIRECTLY INDUCED BY LOCAL CELL-TO-CELL INHIBITION, OR
- DIRECT EFFECT ON NEURON.

4. REDUCED CORTICAL AND FOREBRAIN OUTPUT ACTIVITY RESULTING FROM LOCAL INHIBITION IN AN EFFORT TO ENHANCE ENERGY STORES FOR SURVIVAL.

5. REDUCED FACILITORY RETICULAR FORMATION (MIDBRAIN) OUTPUT ACTIVITY RESULTING FROM LOCAL INHIBITION.

6. LIBERATED INHIBITORY RETICULAR FORMATION (LOWER PONS/MEDULLA) GAINS WIDESPREAD GLOBAL INHIBITORY CONTROL OF THE CORTEX AND FOREBRAIN.

7. SLOW WAVE ACTIVITY RECORDED FROM CORTEX INDICATING GLOBAL *METABOLIC* INHIBITION OF NEURONS TO ENHANCE SURVIVAL IN THE FACE OF ISCHEMIC THREAT.

8. COMPLETE LOSS OF MOTOR CONTROL AND NORMAL CORTICAL INHIBITION OF BRAIN STEM.

9. LOSS OF CONSCIOUSNESS OUTWARD MANIFESTATION OF FUNCTIONAL LOSS OF CORTEX, FOREBRAIN, AND FACILITORY RETICULAR FORMATION (RETICULAR ACTIVATING SYSTEM).

10. BODY ATTEMPTS TO ASSUME HORIZONTAL POSITION WHICH OPTIMIZES RETURN OF BLOOD FLOW FROM HEART TO BRAIN WHEN LOCATED AT THE SAME LEVEL WITHIN THE $+G_z$-FIELD ($+G_z$-EXPOSURE TERMINATED).

B. RECOVERY (Moderate offset of $+G_z$)

11. RETURN OF BLOOD FLOW TO THE CNS:
    - LOWER CENTERS (BRAIN STEM) REPERFUSED FIRST.
    - HIGHER CENTERS (CORTEX) REPERFUSED LAST.

12. INCREASED PERFUSION OF NEURONS RESULTING IN INCREASED FLOW, PERFUSION PRESSURE, OXYGEN, AND GLUCOSE TO NEURONS.

13. LOSS OF LOCAL NEURONAL METABOLIC INHIBITION OF FACILITORY RETICULAR FORMATION (RETICULAR ACTIVATING SYSTEM).

14. RETURN OF FUNCTION FACILITORY RETICULAR FORMATION.

15. OUTPUT ACTIVITY GENERATED IN FACILITORY RETICULAR FORMATION RESULTING IN:
    - IMPULSES TO ACTIVATE FOREBRAIN AND CORTEX, WHICH ARE NOT YET FUNCTIONAL.
    - IMPULSES TO SKELETAL MUSCLES VIA RETICULOSPINAL AND VESTIBULOSPINAL TRACTS PRODUCED MYOCLONIC CONVULSIONS (MYOCLONIC CONVULSIONS SERVE TO CONTRACT MUSCLES THEREBY INCREASING RETURN OF BLOOD FLOW TO THE CNS).

16. SEQUENTIAL REACTIVATION OF FOREBRAIN FOLLOWED BY CORTICAL SYSTEMS THROUGH LOSS OF LOCAL NEURONAL METABOLIC INHIBITION AND GLOBAL INHIBITION BY INHIBITORY RETICULAR FORMATION WITH ACTIVATION FROM FACILITORY RETICULAR FORMATION (RETICULAR ACTIVATING SYSTEM).

17. RETURN OF FUNCTION FOREBRAIN AND CORTICAL CIRCUITS RESPONSIBLE FOR DREAMING STILL WITHOUT HIGHER CORTICAL INHIBITION (DREAMING OCCURS).

18. RETURN OF FUNCTION FOREBRAIN AND CORTICAL CIRCUITS REQUIRED FOR MEMORY (DREAM POTENTIALLY MEMORABLE).

19. CONTINUED PROGRESSION OF CORTICAL FUNCTIONAL RETURN WITH RE-ESTABLISHMENT OF NORMAL BRAIN STEM-CORTICAL FEEDBACK CIRCUITS.

20. CORTICAL INHIBITION CIRCUITS RETURN WITH ALMOST SIMULTANEOUS:
    - FACILITORY RETICULAR FORMATION RE-INHIBITION STOPS MYOCLONIC CONVULSIONS.
    - FOREBRAIN AND LOWER CORTICAL CIRCUIT RE-INHIBITION STOPS DREAMING.
    - SLOW WAVE ACTIVITY RECORDED FROM CORTEX STOPS.
    - CONSCIOUSNESS RETURNS.

21. RETURN OF CORTICAL CONTROL OF MOTOR ACTIVITY.

22. FULL RETURN AND RE-INTEGRATION OF CORTICAL FUNCTION CONTINUES AS CONFUSION AND DISORIENTATION DIMINISHES.

23. RETURN OF NORMAL CNS FUNCTION COMPLETE.

The exact cause of induction of local neuronal metabolic inhibition and recovery of local neuronal activation remains undetermined but may result from perfusion itself, perfusion pressure, oxygen, or other factors. It is more certain in less abrupt forms of anoxic insult, inhibition must result from reduced

oxygen. In G-LOC it is not due to complete depletion of neuronal energy stores, although it may be related to a small but critical reduction in energy. Localized neuronal inhibition precedes complete and integrated (global) system inhibition. EEG data reveals that slow wave activity only occurs during G-LOC exposures with no flat EEG response and no cortical evidence of seizure activity during the myoclonic convulsions. The exact time of onset and recovery of functional and physiologic events derived from G-LOC kinetics may provide the ability to determine the specific biochemical reactions that underlie consciousness based on reaction rates.

It has not escaped my attention that G-LOC kinetics and mechanism have importance relative to understanding our evolutionary pathway. Early evolutionary ischemia when rising to an upright position in the gravitational field could have theoretically resulted in a similar anatomic and physiologic basis for G-LOC and sleep which remove the organism from gravitational ($+G_z$) stress. As upright mammals the primary physiologic stress which has constantly pressured our evolution has been gravitation ($+1G_z$). In some respects it is the body's failure to contend with this stress that constitutes a large portion of human illness. At the end of life it is important to recognize that the psychologic aspects of unconsciousness are, at worst, not the least unpleasant. G-LOC is frequently described as restful and euphoric which may be of interest for understanding near-death phenomenon and managing terminally ill patients.

REFERENCES

1. Whinnery JE, Whinnery AM. Acceleration Induced Loss of Consciousness: A Review of 500 Episodes. Arch. Neurol. 47:464-76; 1990.

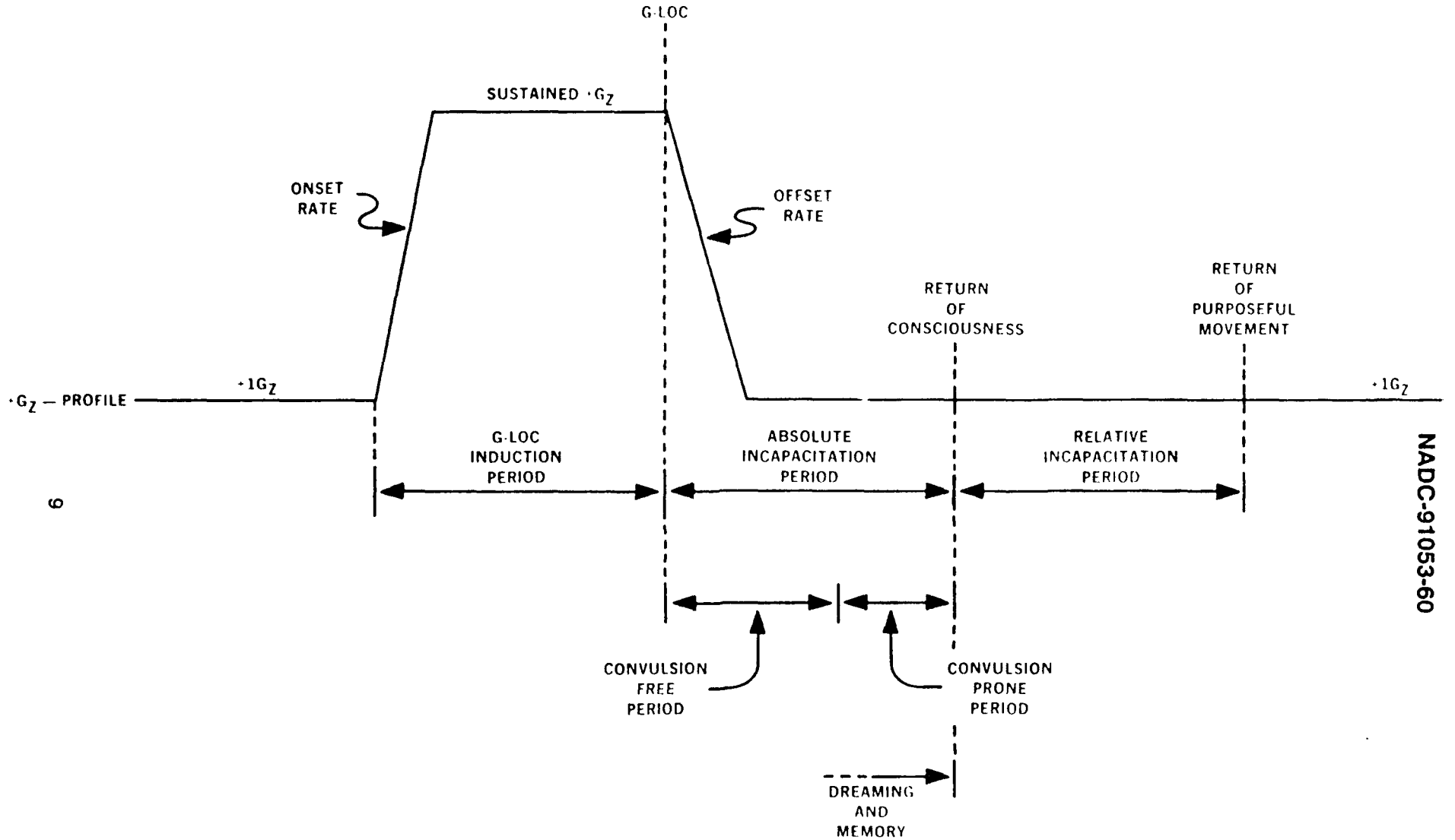


Figure 1. Rapid Onset (>1G/s) $+G_z$-Exposure Profile Resulting In $+G_z$-Induced Loss Of Consciousness (G-LOC) With Kinetically Related Events Including Return Of Consciousness And Return Of Responsiveness And Purposeful Movement

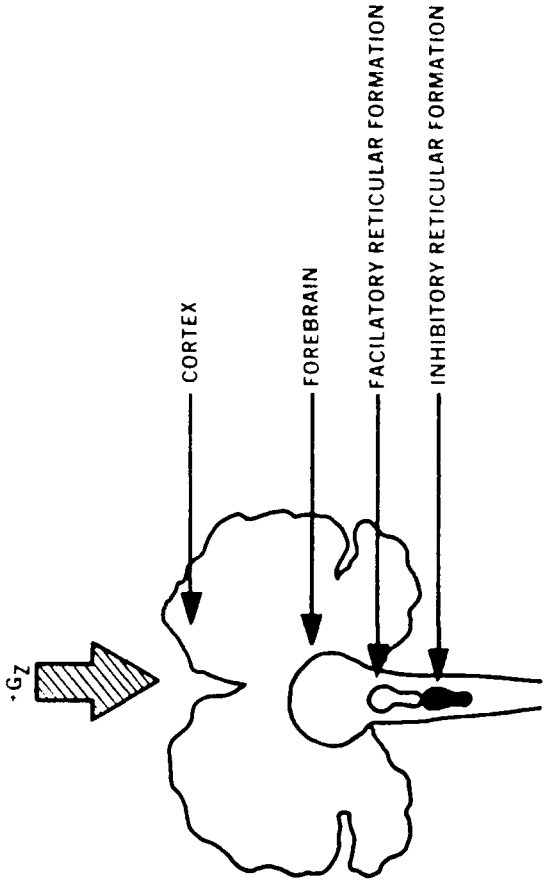
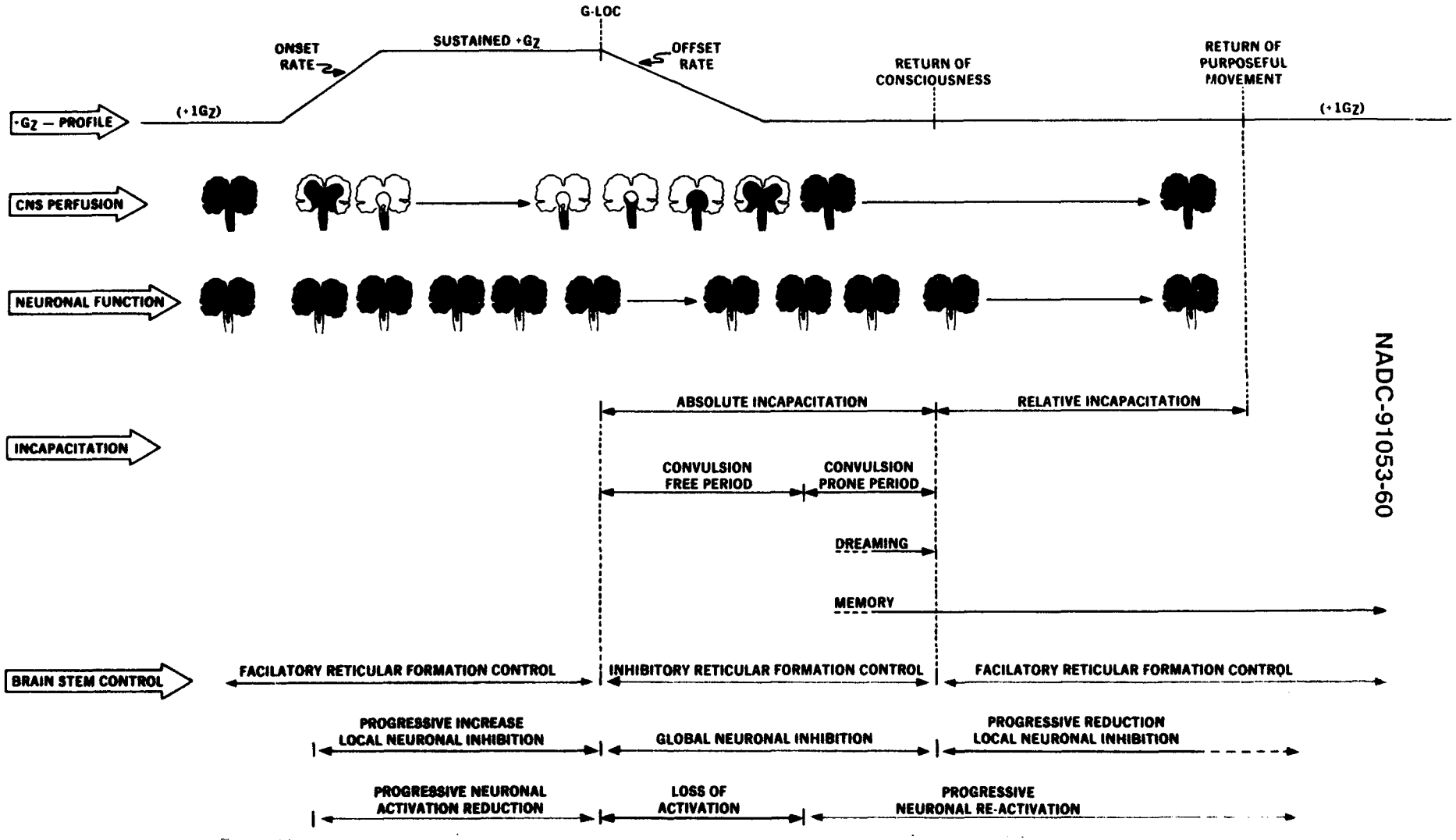


Figure 2. Anatomic Relationship Of The Key Central Nervous System Structures Including The Cortex, Forebrain (Subcortical Structures), And Brain Stem Structures



NADC-91053-60

Figure 3. Postulated Relationship Between $+G_z$-Induced Ischemia And Neurophysiology Which Produce The Observed Symptoms Associated With G-LOC